GenCore version 5.1.6

OM nucleic - protein search, using frame_plus_n2p model

Run on: February 9, 2005, 17:36:14 ; Search time 0.5 Seconds
(without alignments)
1.742 Million cell updates/sec

Title: US-09-824-134-1
Perfect score: 3092
Sequence: 1 GTGAATCAGGCACCGGAGTG.....ACAAAAAAAAAAAAAAAAAA 1701

Scoring table: BLOSUM62
Xgapop 10.0 , Xgapext 0.5
Ygapop 10.0 , Ygapext 0.5
Fgapop 6.0 , Fgapext 7.0
Delop 6.0 , Delext 7.0

Searched: 1 seqs, 256 residues

Total number of hits satisfying chosen parameters: 2

Minimum DB seq length: 0
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%
Maximum Match 100%
Listing first 45 summaries

Command line parameters:
-MODEL=frame+_n2p.model -DEV=soft -Q=US09824134.seq -DB=US09824134.pep
-SUFFIX=pto -OUT=US09824134-1and2.align -MINMATCH=0.1 -LOOPCL=0 -LOOPEXT=0
-UNITS=bits -START=1 -END=-1 -MATRIX=blosum62 -TRANS=human40.cdi -LIST=45
-DOCALIGN=200 -THR_SCORE=pct -THR_MAX=100 -THR_MIN=0 -ALIGN=15 -MODE=LOCAL
-OUTFMT=pto -NORM=ext -HEAPSIZE=500 -MINLEN=0 -MAXLEN=2000000000 -NCPU=6
-NO_XLPXY -NEG_SCORES=0 -LONGLOG -THREADS=1 -XGAPOP=10 -XGAPEXT=0.5 -FGAPOP=6
-FGAPEXT=7 -YGAPOP=10 -YGAPEXT=0.5 -DELOP=6 -DELEXT=7

Database : US09824134.pep:*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	% Query Match	Length	DB	ID	Description
1	1302	42.1	256	1	US-09-824-134-2	Sequence 2, Appli
c 2	48	1.6	256	1	US-09-824-134-2	Sequence 2, Appli

ALIGNMENTS

RESULT 1
US-09-824-134-2
; Sequence 2, Application US/09824134
; GENERAL INFORMATION:
; APPLICANT: WALLACH, David
; BOLDIN, Mark
; VARFOLOMEEV, Eugene
; METT, Igor
; TITLE OF INVENTION: MODULATORS OF THE FUNCTION OF FAS/APO1
; RECEPTORS
; NUMBER OF SEQUENCES: 2
; CORRESPONDENCE ADDRESS:
; ADDRESSEE: BROWDY AND NEIMARK, P.L.L.C.
; STREET: 419 Seventh Street N.W., Ste. 300
; CITY: Washington
; STATE: D.C.
; COUNTRY: United States of America
; ZIP: 20004
; COMPUTER READABLE FORM:
; MEDIUM TYPE: Floppy disk
; COMPUTER: IBM PC compatible
; OPERATING SYSTEM: PC-DOS/MS-DOS
; SOFTWARE: PatentIn Release #1.0, Version #1.30
; CURRENT APPLICATION DATA:
; APPLICATION NUMBER: US/09/824,134
; FILING DATE: 03-Apr-2001
; PRIOR APPLICATION DATA:
; APPLICATION NUMBER: 08/860,082
; FILING DATE: <Unknown>
; APPLICATION NUMBER: IL 112022
; FILING DATE: 15-DEC-1994
; APPLICATION NUMBER: IL 112692
; FILING DATE: 19-FEB-1995
; APPLICATION NUMBER: IL 114615
; FILING DATE: 16-JUL-1995
; ATTORNEY/AGENT INFORMATION:
; NAME: BROWDY, Roger L.
; REGISTRATION NUMBER: 25,618
; REFERENCE/DOCKET NUMBER: WALLACH=16
; TELECOMMUNICATION INFORMATION:
; TELEPHONE: (202) 628-5197
; TELEFAX: (202) 737-3528
; INFORMATION FOR SEQ ID NO: 2:
; SEQUENCE CHARACTERISTICS:
; LENGTH: 256 amino acids
; TYPE: amino acid
; TOPOLOGY: linear
; MOLECULE TYPE: protein
; SEQUENCE DESCRIPTION: SEQ ID NO: 2:
US-09-824-134-2

Alignment Scores:

Pred. No.:	0	Length:	256
Score:	1302.00	Matches:	256
Percent Similarity:	100.00%	Conservative:	0
Best Local Similarity:	100.00%	Mismatches:	0
Query Match:	42.11%	Indels:	0
DB:	1	Gaps:	0

US-09-824-134-1 (1-1701) x US-09-824-134-2 (1-256)

```
Qy          1 GTGAATCAGGCACCGGAGTGCAGGTTCGGGGGTGGAATCCTTGGGCCGCTGGGCAAGCGG 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 ValAsnGlnAlaProGluCysArgPheGlyGlyGlyIleLeuGlyProLeuGlyLysArg 20

Qy         61 CGAGACCTGGCCAGGGCCAGCGAGCCGAGGACAGAGGGCGCGCGGAGGGCCGGGCCGCAG 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         21 ArgAspLeuAlaArgAlaSerGluProArgThrGluGlyAlaArgArgAlaGlyProGln 40

Qy        121 CCCCGGCCGCTTGCAGACCCCGCCATGGACCCGTTCCTGGTGCTGCTGCACTCGGTGTCG 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         41 ProArgProLeuAlaAspProAlaMetAspProPheLeuValLeuLeuHisSerValSer 60

Qy        181 TCCAGCCTGTCGAGCAGCGAGCTGACCGAGCTCAAGTTCCTATGCCTCGGGCGCGTGGTC 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 SerSerLeuSerSerSerGluLeuThrGluLeuLysPheLeuCysLeuGlyArgValVal 80

Qy        241 AAGCGCAAGCTGGAGCGCGTGCAGAGCGGCCTAGACCTCTTCTCCATGCTGCTGGAGCAG 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         81 LysArgLysLeuGluArgValGlnSerGlyLeuAspLeuPheSerMetLeuLeuGluGln 100

Qy        301 AACGACCTGGAGCCCGGGCACACCGAGCTCCTGCGCGAGCTGCTCGCCTCCCTGCGGCGC 360
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        101 AsnAspLeuGluProGlyHisThrGluLeuLeuArgGluLeuLeuAlaSerLeuArgArg 120

Qy        361 CACGACCTGCTGCGGCGCGTCGACGACTTCGAGGCGGGGGCGGCGGCCGGGGCCGCGCCT 420
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 HisAspLeuLeuArgArgValAspAspPheGluAlaGlyAlaAlaAlaGlyAlaAlaPro 140
```

```
Qy        421 GGGGAAGAAGACCTGTGTGCAGCATTTAACGTCATATGTGATAATGTGGGGAAAGATTGG 480
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        141 GlyGluGluAspLeuCysAlaAlaPheAsnValIleCysAspAsnValGlyLysAspTrp 160

Qy        481 AGAAGGCTGGCTCGTCAGCTCAAAGTCTCAGACACCAAGATCGACAGCATCGAGGACAGA 540
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        161 ArgArgLeuAlaArgGlnLeuLysValSerAspThrLysIleAspSerIleGluAspArg 180

Qy        541 TACCCCCGCAACCTGACAGAGCGTGTGCGGGAGTCACTGAGAATCTGGAAGAACACAGAG 600
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 TyrProArgAsnLeuThrGluArgValArgGluSerLeuArgIleTrpLysAsnThrGlu 200

Qy        601 AAGGAGAACGCAACAGTGGCCCACCTGGTGGGGGCTCTCAGGTCCTGCCAGATGAACCTG 660
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        201 LysGluAsnAlaThrValAlaHisLeuValGlyAlaLeuArgSerCysGlnMetAsnLeu 220

Qy        661 GTGGCTGACCTGGTACAAGAGGTTCAGCAGGCCCGTGACCTCCAGAACAGGAGTGGGGCC 720
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        221 ValAlaAspLeuValGlnGluValGlnGlnAlaArgAspLeuGlnAsnArgSerGlyAla 240

Qy        721 ATGTCCCCGATGTCATGGAACTCAGACGCATCTACCTCCGAAGCGTCC 768
              ||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 MetSerProMetSerTrpAsnSerAspAlaSerThrSerGluAlaSer 256

RESULT 2
US-09-824-134-2
; Sequence 2, Application US/09824134
;   GENERAL INFORMATION:
;        APPLICANT: WALLACH, David
;                   BOLDIN, Mark
;                   VARFOLOMEEV, Eugene
;                   METT, Igor
;        TITLE OF INVENTION: MODULATORS OF THE FUNCTION OF FAS/APO1
;                            RECEPTORS
;        NUMBER OF SEQUENCES: 2
;        CORRESPONDENCE ADDRESS:
;             ADDRESSEE: BROWDY AND NEIMARK, P.L.L.C.
;             STREET: 419 Seventh Street N.W., Ste. 300
;             CITY: Washington
;             STATE: D.C.
;             COUNTRY: United States of America
;             ZIP: 20004
;        COMPUTER READABLE FORM:
;             MEDIUM TYPE: Floppy disk
;             COMPUTER: IBM PC compatible
;             OPERATING SYSTEM: PC-DOS/MS-DOS
;             SOFTWARE: PatentIn Release #1.0, Version #1.30
;        CURRENT APPLICATION DATA:
;             APPLICATION NUMBER: US/09/824,134
;             FILING DATE: 03-Apr-2001
;        PRIOR APPLICATION DATA:
;             APPLICATION NUMBER: 08/860,082
;             FILING DATE: <Unknown>
;             APPLICATION NUMBER: IL 112022
;             FILING DATE: 15-DEC-1994
;             APPLICATION NUMBER: IL 112692
;             FILING DATE: 19-FEB-1995
;             APPLICATION NUMBER: IL 114615
;             FILING DATE: 16-JUL-1995
;        ATTORNEY/AGENT INFORMATION:
;             NAME: BROWDY, Roger L.
;             REGISTRATION NUMBER: 25,618
;             REFERENCE/DOCKET NUMBER: WALLACH=16
;        TELECOMMUNICATION INFORMATION:
;             TELEPHONE: (202) 628-5197
;             TELEFAX: (202) 737-3528
;   INFORMATION FOR SEQ ID NO: 2:
;        SEQUENCE CHARACTERISTICS:
;             LENGTH: 256 amino acids
;             TYPE: amino acid
;             TOPOLOGY: linear
;        MOLECULE TYPE: protein
;        SEQUENCE DESCRIPTION: SEQ ID NO: 2:
US-09-824-134-2

Alignment Scores:
Pred. No.:                0              Length:          256
Score:                    48.00          Matches:         33
Percent Similarity:       36.44%         Conservative:    10
Best Local Similarity:    27.97%         Mismatches:      49
Query Match:              1.57%          Indels:          26
DB:                       1              Gaps:            6

US-09-824-134-1 (1-1701) x US-09-824-134-2 (1-256)

Qy        434 AGGTCTTCTTCCCCAGGCGCGGCCCCGGCCGCCGCCCCCGCCTCGAAGTCGTCGACGCGC 375
              |||   :::   |||         |||   |||   ||||||
Db         35 ArgArgAlaGlyProGlnProArgProLeuAlaAspProAlaMetAspProPheLeuVal 54

Qy        374 CGCAGCAGGTCGTGGCGCCGCAGGGAGGCGAGCAGCTCGCGCAGGAGCTCGGTGTGCCCG 315
                  |||                 |||||||||     ||||||
Db         55 LeuLeuHisSer--------------ValSerSerSerLeuSerSerSerGluLeuThr 69

Qy        314 GGCTCCAGGTCGTTCTGCTCCAGCAGCATGGAGAAGAGGTCTAGGCCGCTCTGCACGCGC 255
                :::     |||         :::   ||||||                    :::
Db         70 GluLeuLysPheLeuCysLeuGlyArgValValLysArgLysLeuGluArg---ValGln 88

Qy        254 TCCAGCTTGCGCTTGACCACG----------------------CGCCCGAGGCATAGG 219
              |||   |||   |||   :::                        |||   |||
Db         89 SerGlyLeuAspLeuPheSerMetLeuLeuGluGlnAsnAspLeuGluProGlyHisThr 108

Qy        218 AAC--------------TTGAGCTCGGTC------AGCTCGCTGCTCGACAGGCTGGAC 180
                             |||:::|||:::          ||||||   |||:::|||
Db        109 GluLeuLeuArgGluLeuLeuAlaSerLeuArgArgHisAspLeuLeuArgArgValAsp 128

Qy        179 GACACCGAGTGCAGCAGCACCAGGAACGGGTCCATGGCGGGGTCTGCAAGCGGC 126
              |||   |||                 |||:::   ||||||:::|||   |||
Db        129 AspPheGluAla--------------GlyAlaAlaAlaGlyAlaAlaProGly 141

Search completed: February  9, 2005, 17:36:15
Job time : 0.5 secs
```

GenCore version 5.1.6

OM protein - protein search, using sw model

Run on: February 11, 2005, 11:53:56 ; Search time 74 Seconds
(without alignments)
606.273 Million cell updates/sec

Title: US-09-824-134-2_COPY_130_245
Perfect score: 593
Sequence: 1 FEAGAAAGAAPGEEDLCAAF.....QEVQQARDLQNRSGAMSPMS 116

Scoring table: BLOSUM62
Gapop 10.0 , Gapext 0.5

Searched: 2105692 seqs, 386760381 residues

Total number of hits satisfying chosen parameters: 2105692

Minimum DB seq length: 0
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%
Maximum Match 100%
Listing first 45 summaries

Database : A_Geneseq_16Dec04:*
1: geneseqp1980s:*
2: geneseqp1990s:*
3: geneseqp2000s:*
4: geneseqp2001s:*
5: geneseqp2002s:*
6: geneseqp2003as:*
7: geneseqp2003bs:*
8: geneseqp2004s:*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	% Query Match	Length	DB	ID	Description
1	593	100.0	208	2	AAW03653	Aaw03653 FADD (Fas
2	593	100.0	208	2	AAW96154	Aaw96154 Human FAD
3	593	100.0	208	3	AAY51329	Aay51329 Human FAD
4	593	100.0	208	4	AAB84804	Aab84804 Human FAD
5	593	100.0	208	6	ABR62711	Abr62711 Human FAD
6	593	100.0	208	7	ADD25629	Add25629 Binding d
7	593	100.0	208	7	ADD25623	Add25623 Binding d
8	593	100.0	208	8	ABM81285	Abm81285 Tumour-as
9	593	100.0	208	8	ADS88167	Ads88167 Human pro
10	593	100.0	211	7	ADD25847	Add25847 Binding d
11	593	100.0	256	2	AAR98346	Aar98346 MORT-1 mo
12	593	100.0	256	2	AAW11894	Aaw11894 Modulator
13	589	99.3	201	2	AAW87492	Aaw87492 Amino aci
14	589	99.3	208	2	AAW87493	Aaw87493 Amino aci
15	586	98.8	201	2	AAW87491	Aaw87491 Amino aci
16	586	98.8	208	4	AAB61119	Aab61119 Human FAD
17	382.5	64.5	205	4	AAB61900	Aab61900 Mouse apo
18	382.5	64.5	210	7	ADD25857	Add25857 Binding d
19	382	64.4	74	6	ADA49711	Ada49711 Death dom
20	380.5	64.2	205	6	ABR62712	Abr62712 Mouse FAD
21	357.5	60.3	117	4	AAB61902	Aab61902 Mouse apo
22	351	59.2	95	5	ABG75682	Abg75682 Fas-assoc
23	346	58.3	99	5	ABB81754	Abb81754 Tumour ne
24	331	55.8	93	5	ABG75684	Abg75684 Fas-assoc
25	331	55.8	93	5	ABG75685	Abg75685 Fas-assoc
26	325	54.8	93	5	ABG75683	Abg75683 Fas-assoc
27	318	53.6	62	2	AAW00210	Aaw00210 Human MOR
28	136.5	23.0	88	7	ADG42592	Adg42592 NOV1 doma
29	131	22.1	75	7	ADG42594	Adg42594 NOV1 doma
30	115.5	19.5	656	2	AAW04627	Aaw04627 Mouse rec
31	115.5	19.5	656	2	AAW80994	Aaw80994 Human rec
32	114.5	19.3	1034	8	ADR08537	Adr08537 Human pro
33	114.5	19.3	1536	6	ABU11523	Abu11523 Human MDD
34	114.5	19.3	1880	8	ADR90358	Adr90358 Full leng
35	114.5	19.3	1881	7	ADD47763	Add47763 Human Pro
36	114	19.2	239	4	ABB62302	Abb62302 Drosophil
37	111.5	18.8	99	7	ADC08901	Adc08901 Recombina
38	111.5	18.8	100	7	ADC08899	Adc08899 Recombina
39	111.5	18.8	273	7	ADM05095	Adm05095 Human pro
40	111.5	18.8	671	2	AAW15461	Aaw15461 Human rec
41	111.5	18.8	671	2	AAW04628	Aaw04628 Human rec
42	111.5	18.8	671	3	AAY78502	Aay78502 Human RIP
43	111.5	18.8	671	4	AAB82091	Aab82091 Human Rec
44	111.5	18.8	671	4	ABG16302	Abg16302 Novel hum
45	111.5	18.8	671	5	AAU80370	Aau80370 Human cel

ALIGNMENTS

RESULT 1
AAW03653
ID AAW03653 standard; protein; 208 AA.
XX
AC AAW03653;
XX
DT 22-FEB-1997 (first entry)
XX
DE FADD (Fas-associating protein with novel death domain) protein.
XX
KW Human; FADD; Fas-associating protein with novel death domain; apoptosis;
KW Fas receptor; death domain; gene therapy; antibody; immunoassay;
KW drug screening; diagnostic; AIDS; antiinflammatory; antitumour;
KW cerebroprotective; neuroprotective.
XX
OS Homo sapiens.
XX
FH Key Location/Qualifiers
FT Region 1. .125
FT /note= "N-terminal fragment, inducing apoptosis but not
FT binding to Fas receptor"
FT Region 35. .208
FT /note= "C-terminal active fragment"
FT Region 41. .208
FT /note= "C-terminal active fragment"
FT Region 42. .208
FT /note= "Fas receptor-binding NFD-2 polypeptide"
FT Region 61. .208
FT /note= "Fas receptor-binding NFD-3 polypeptide"
FT Region 80. .208
FT /note= "Fas receptor-binding NFD-4 polypeptide"
FT Domain 111. .177
FT /note= "Death domain"
FT Misc-difference 121
FT /note= "Altered to Asn in FADDmt mutant"
XX
PN WO9631603-A2.
XX
PD 10-OCT-1996.
XX
PF 28-FEB-1996; 96WO-US002857.
XX
PR 03-APR-1995; 95US-00416379.
PR 18-MAY-1995; 95US-00443982.
XX
PA (UNMI) UNIV MICHIGAN.
XX
PI Dixit VM, Orourke K;

XX
DR WPI; 1996-465026/46.
DR N-PSDB; AAT39397.
XX
PT FADD protein that binds to cytoplasmic region of Fas receptor - for
PT identifying inhibitors of Fas-associated apoptosis useful for treating
PT e.g. AIDS, leukaemia, stroke, etc.
XX
PS Example 1; Fig 2A-B; 96pp; English.
XX
CC The sequence corresponds to FADD (Fas-associating protein with novel
CC death domain), which binds the cytoplasmic region of a Fas receptor, and
CC modulates apoptosis induced by activation of the receptor by ligand
CC binding. The FADD cDNA has been isolated using a yeast two-hybrid system
CC to screen for proteins interacting with the Fas cytoplasmic domain. The
CC protein contains a death domain, with interacts with the death domain of
CC Fas. Mutation of Val-121 to Asn in mutant FADDmt disrupts binding and/or
CC signalling properties. C-terminal polypeptides NFD-2, NFD-3 and NFD-4
CC bind the Fas receptor cytoplasmic domain in vitro. An N-terminal fragment
CC induces apoptosis but does not bind the Fas receptor. The encoding DNA
CC may be used in gene therapy, and the protein or a corresponding antibody
CC may be used to screen for agents modulating FADD pathway cellular
CC functions and Fas-associated apoptosis, for use in therapy of e.g. AIDS,
CC inflammation, leukaemia, myocardial infarction, degenerative disease, etc
XX
SQ Sequence 208 AA;

Query Match 100.0%; Score 593; DB 2; Length 208;
Best Local Similarity 100.0%; Pred. No. 1.9e-63;
Matches 116; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 FEAGAAAGAAPGEEDLCAAFNVICDNVGKDWRRLARQLKVSDTKIDSIEDRYPRNLTERV 60
Db 82 FEAGAAAGAAPGEEDLCAAFNVICDNVGKDWRRLARQLKVSDTKIDSIEDRYPRNLTERV 141

Qy 61 RESLRIWKNTEKENATVAHLVGALRSCQMNLVADLVQEVQQARDLQNRSGAMSPMS 116
Db 142 RESLRIWKNTEKENATVAHLVGALRSCQMNLVADLVQEVQQARDLQNRSGAMSPMS 197

RESULT 2
AAW96154
ID AAW96154 standard; protein; 208 AA.
XX
AC AAW96154;
XX
DT 27-APR-1999 (first entry)
XX
DE Human FADD protein.
XX
KW FIP; FADD interacting protein; FADD;
KW Fas-associated protein with a novel death domain; cell death; apoptosis;
KW Alzheimer's disease; Acquired Immune Deficiency Syndrome; AIDS;
KW muscular dystrophy; amyotrophic lateral sclerosis; virus; bacteria;
KW fungus; mycoplasm; protozoa; neoplasia; dysplasia; hyperplasia.
XX
OS Homo sapiens.
XX
PN WO9900499-A1.
XX
PD 07-JAN-1999.
XX
PF 26-JUN-1998; 98WO-US013320.
XX
PR 26-JUN-1997; 97US-0050792P.
PR 03-JUN-1998; 98US-0087886P.
XX
PA (CHIR) CHIRON CORP.
XX
PI Chen TT, Williams LT;
XX
DR WPI; 1999-095745/08.
DR N-PSDB; AAX08910.
XX
PT New FADD (Fas-associated protein with a novel death domain)-Interacting
PT Protein - useful for inducing or preventing apoptosis in a cell, to aid
PT in controlling apoptosis-related diseases.
XX
PS Disclosure; Page 47; 58pp; English.
XX
CC An epitope of human FADD (Fas-associated protein with a novel death
CC domain)-Interacting protein (FIP protein) comprising amino acids 348-727
CC of the protein described in AAW96153, can be used to induce or prevent
CC apoptosis in a cell. Specifically, decreasing the levels of FIP348-727
CC prevents apoptosis. This is useful in cells which are dying prematurely,
CC eg: Alzheimer's disease, Acquired Immune Deficiency Syndrome (AIDS),
CC muscular dystrophy, amyotrophic lateral sclerosis (and other muscle
CC wasting diseases), autoimmune diseases, and diseases where cells are
CC infected with a pathogen (virus, bacteria, fungus, mycoplasm or
CC protozoa). Increasing the levels of FIP 348-727 induces apoptosis which
CC is useful in cells suffering from neoplasias, dysplasias, hyperplasias,
CC or their symptoms. Purified and isolated FIP subgenomic polynucleotides
CC are useful as primers to obtain more copies of the nucleotides, and as
CC probes that identify wild-type or mutant coding sequences. They are also
CC useful for expressing FIP mRNA, proteins or fusion proteins, and in the
CC generation of FIP antisense oligonucleotides and ribozymes. They are also
CC useful in expression constructs and in gene delivery vehicles (optionally
CC in combination with a condensing agent) that deliver FIP mRNA or
CC oligonucleotides, FIP proteins (including variants), FIP-specific
CC ribozymes or single-chain antibodies into eukaryotic cells. This is the
CC human FADD protein. Human FIP protein binds to amino acids 1-110 of this
CC sequence
XX
SQ Sequence 208 AA;

Query Match 100.0%; Score 593; DB 2; Length 208;
Best Local Similarity 100.0%; Pred. No. 1.9e-63;
Matches 116; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 FEAGAAAGAAPGEEDLCAAFNVICDNVGKDWRRLARQLKVSDTKIDSIEDRYPRNLTERV 60
Db 82 FEAGAAAGAAPGEEDLCAAFNVICDNVGKDWRRLARQLKVSDTKIDSIEDRYPRNLTERV 141

Qy 61 RESLRIWKNTEKENATVAHLVGALRSCQMNLVADLVQEVQQARDLQNRSGAMSPMS 116
Db 142 RESLRIWKNTEKENATVAHLVGALRSCQMNLVADLVQEVQQARDLQNRSGAMSPMS 197

RESULT 3
AAY51329
ID AAY51329 standard; protein; 208 AA.
XX
AC AAY51329;
XX
DT 19-APR-2000 (first entry)
XX
DE Human FADD protein.
XX
KW FADD; human; antisense; inhibitor; Fas-associated death domain.
XX
OS Homo sapiens.
XX
PN US6015712-A.
XX
PD 18-JAN-2000.
XX
PF 19-JUL-1999; 99US-00357072.
XX
PR 19-JUL-1999; 99US-00357072.
XX
PA (ISIS-) ISIS PHARM INC.
XX
PI Monia BP, Cowsert LM, Baker BF, Zhang H;
XX
DR WPI; 2000-126316/11.
DR N-PSDB; AAZ44745.

XX
PT Antisense oligonucleotides, useful for inhibiting human Fas-associated
PT death domain (FADD) expression are targeted to the 3' untranslated region
PT of the FADD gene.
XX
PS Example 13; Col 43-46; 37pp; English.
XX
CC This invention describes novel antisense oligonucleotides (OGNs) (I) 8-20
CC nucleotides in length that specifically hybridize with and inhibit
CC nucleic acids encoding human Fas-associated death domain (FADD), targeted
CC to the 3' untranslated region (3'UTR). (I) can be used to treat animals,
CC especially humans, suspected of having or being prone to a disease or
CC condition associated with FADD expression. This sequence represents the
CC human FADD protein described in the method of the invention
XX
SQ Sequence 208 AA;

Query Match 100.0%; Score 593; DB 3; Length 208;
Best Local Similarity 100.0%; Pred. No. 1.9e-63;
Matches 116; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 FEAGAAAGAAPGEEDLCAAFNVICDNVGKDWRRLARQLKVSDTKIDSIEDRYPRNLTERV 60
Db 82 FEAGAAAGAAPGEEDLCAAFNVICDNVGKDWRRLARQLKVSDTKIDSIEDRYPRNLTERV 141

Qy 61 RESLRIWKNTEKENATVAHLVGALRSCQMNLVADLVQEVQQARDLQNRSGAMSPMS 116
Db 142 RESLRIWKNTEKENATVAHLVGALRSCQMNLVADLVQEVQQARDLQNRSGAMSPMS 197

RESULT 4
AAB84804
ID AAB84804 standard; protein; 208 AA.
XX
AC AAB84804;
XX
DT 12-JUL-2001 (first entry)
XX
DE Human FADD prodomain.
XX
KW NF-kappaB; JNK; apoptosis; death effector domain; DED.
XX
OS Homo sapiens.
XX
PN US6207458-B1.
XX
PD 27-MAR-2001.
XX
PF 07-MAY-1998; 98US-00074044.
XX
PR 07-MAY-1998; 98US-00074044.
XX
PA (UNIW) UNIV WASHINGTON.
XX
PI Chaudhary PM, Hood L;
XX
DR WPI; 2001-342087/36.
XX
PT Testing candidate compound affecting cellular NFkappaB JNK, apoptosis
PT activity by comparing cell activity in presence and absence of
PT proteinaceous species having two death effector domain and test compound.
XX
PS Disclosure; Col 51-52; 62pp; English.
XX
CC The present invention relates to testing candidate compounds to determine
CC whether they affect NF-kappaB, JNK and apoptosis activity. The method
CC involves the use of 2 death effector domains (DED). The The compounds
CC identified by the invention have therapeutic applications and are useful
CC for regulating cellular NFkappaB, JNK and apoptosis activity. The assay
CC is useful for identifying pharmacological agents or lead compounds
CC generally involved in assaying for compounds which regulate or modulate a
CC cell activity. The present sequence is a prodoamin used in the invention
XX
SQ Sequence 208 AA;

Query Match 100.0%; Score 593; DB 4; Length 208;
Best Local Similarity 100.0%; Pred. No. 1.9e-63;
Matches 116; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 FEAGAAAGAAPGEEDLCAAFNVICDNVGKDWRRLARQLKVSDTKIDSIEDRYPRNLTERV 60
Db 82 FEAGAAAGAAPGEEDLCAAFNVICDNVGKDWRRLARQLKVSDTKIDSIEDRYPRNLTERV 141

Qy 61 RESLRIWKNTEKENATVAHLVGALRSCQMNLVADLVQEVQQARDLQNRSGAMSPMS 116
Db 142 RESLRIWKNTEKENATVAHLVGALRSCQMNLVADLVQEVQQARDLQNRSGAMSPMS 197

RESULT 5
ABR62711
ID ABR62711 standard; protein; 208 AA.
XX
AC ABR62711;
XX
DT 06-NOV-2003 (first entry)
XX
DE Human FADD.
XX
KW FADD; human; tumour; marker; diagnosis; prognosis; thyroid.
XX
OS Homo sapiens.
XX
PN WO2003056340-A2.
XX
PD 10-JUL-2003.
XX
PF 23-DEC-2002; 2002WO-EP014906.
XX
PR 24-DEC-2001; 2001EP-00403359.
PR 22-OCT-2002; 2002EP-00292619.
XX
PA (INRM) INSERM INST NAT SANTE & RECH MEDICALE.
PA (CNRS) CNRS CENT NAT RECH SCI.
XX
PI Chiocchia G, Tourneur L, Feunteun J, Michiels F, Buzyn A;
XX
DR WPI; 2003-645962/61.
XX
PT Use of Fas associated protein with dead domain, and cellular
PT phosphorylated p38-mitogen activated protein kinases as a biological
PT indicator of tumor status.
XX
PS Disclosure; Fig 7; 118pp; English.
XX
CC The present sequence is the protein sequence of human Fas-associated
CC protein with death domain (FADD). The invention relates to the use of
CC FADD and phosphorylated p38-MAPK as markers for the absence of in vivo
CC tumour. This use may be complemented by the use of the Fas ligand (FasL)
CC as a marker for presence of in vivo tumour. The amounts of FADD proteins
CC and phosphorylated p38-MAPK decrease, sometimes down to zero, with tumour
CC development, while FasL expression is gained. FADD proteins are secreted
CC from tumour cells. A low cellular amount and a high extracellular amount
CC of FADD proteins are prognostic of resistance to chemotherapy. The
CC invention provides methods for determining a status of tumour
CC absence/presence, and for prognosis of the resistance of a tumour to
CC chemotherapy on the basis of these findings
XX
SQ Sequence 208 AA;

Query Match 100.0%; Score 593; DB 6; Length 208;
Best Local Similarity 100.0%; Pred. No. 1.9e-63;
Matches 116; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 FEAGAAAGAAPGEEDLCAAFNVICDNVGKDWRRLARQLKVSDTKIDSIEDRYPRNLTERV 60
Db 82 FEAGAAAGAAPGEEDLCAAFNVICDNVGKDWRRLARQLKVSDTKIDSIEDRYPRNLTERV 141

```
Qy         61 RESLRIWKNTEKENATVAHLVGALRSCQMNLVADLVQEVQQARDLQNRSGAMSPMS 116
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        142 RESLRIWKNTEKENATVAHLVGALRSCQMNLVADLVQEVQQARDLQNRSGAMSPMS 197
```

RESULT 6
ADD25629
ID ADD25629 standard; protein; 208 AA.
XX
AC ADD25629;
XX
DT 15-JAN-2004 (first entry)
XX
DE Binding domain-immunoglobulin fusion protein-associated protein #92.
XX
KW Binding domain; immunoglobulin; fusion protein; cytostatic;
KW antiarthritic; immunosuppressive; antidiabetic; antithyroid;
KW neuroprotective; hinge region; immunoglobulin heavy chain;
KW CH2 constant region; CH3 constant region; IgG1;
KW antibody dependent cell-mediated cytotoxicity; ADCC; complement fixation;
KW malignant condition; B-cell disorder; melanoma; carcinoma; sarcoma;
KW rheumatoid arthritis; myasthenia gravis; Grave's disease;
KW type I diabetes mellitus; multiple sclerosis; autoimmune disease.
XX
OS Unidentified.
XX
PN US2003118592-A1.
XX
PD 26-JUN-2003.
XX
PF 25-JUL-2002; 2002US-00207655.
XX
PR 17-JAN-2001; 2001US-0367358P.
PR 17-JAN-2002; 2002US-00053530.
PR 03-JUN-2002; 2002US-0385691P.
XX
PA (GENE-) GENECRAFT INC.
XX
PI Ledbetter JA, Hayden-Ledbetter MS, Thompson PA;
XX
DR WPI; 2003-801317/75.
XX
PT New binding domain-immunoglobulin fusion protein, useful for treating a
PT subject having or suspected of having a malignant condition or a B-cell
PT disorder, e.g. melanoma, Grave's disease or autoimmune disease.
XX
PS Disclosure; SEQ ID NO 190; 157pp; English.
XX
CC The invention relates to a binding domain-immunoglobulin fusion protein
CC comprising a binding domain polypeptide that is fused to an
CC immunoglobulin hinge region polypeptide, an immunoglobulin heavy chain
CC CH2 constant region polypeptide that is fused to the hinge region
CC polypeptide, and an immunoglobulin heavy chain CH3 constant region
CC polypeptide that is fused to the CH2 constant region polypeptide. The
CC hinge region polypeptide comprises: a wild-type human IgG1 immunoglobulin
CC hinge region polypeptide; a mutated human IgG1 immunoglobulin hinge
CC region polypeptide, derived from (a) having 3 or more cysteine residues;
CC where the mutated human IgG1 immunoglobulin hinge region polypeptide
CC contains 2 cysteine residues, where the first cysteine is not mutated; a
CC mutated human IgG1 immunoglobulin hinge region polypeptide, derived from
CC (a) having 3 or more cysteine residues, where the mutated human IgG1
CC immunoglobulin hinge region polypeptide contains no more than one
CC cysteine residue; and a mutated human IgG1 immunoglobulin hinge region
CC polypeptide, derived from (a) having 3 or more cysteine residues; where
CC the mutated human IgG1 immunoglobulin hinge region polypeptide contains
CC no cysteine residues. The binding domain-immunoglobulin fusion protein is
CC capable of at least one immunological activity comprising antibody
CC dependent cell-mediated cytotoxicity (ADCC) and complement fixation. The
CC binding domain polypeptide is capable of specifically binding to an
CC antigen. Also included are an isolated polynucleotide encoding the
CC binding domain-immunoglobulin fusion protein, a recombinant expression
CC construct comprising the polynucleotide (operably linked to a promoter),
CC a host cell transformed or transfected with a recombinant expression
CC construct, producing the binding domain-immunoglobulin fusion protein, a
CC pharmaceutical composition comprising the binding domain-immunoglobulin
CC fusion protein or polynucleotide and a carrier, and treating a subject
CC having or suspected of having a malignant condition or a B-cell disorder.
CC The binding domain-immunoglobulin fusion protein is useful for treating a
CC subject having or suspected of having a malignant condition or a B-cell
CC disorder, e.g. melanoma, carcinoma or sarcoma, rheumatoid arthritis,
CC myasthenia gravis, Grave's disease, type I diabetes mellitus, multiple
CC sclerosis or autoimmune disease. The present sequence is a binding domain
CC -immunoglobulin fusion protein-associated protein sequence. Note: The
CC sequence data for this patent formed part of the printed specification
CC and is also available in electronic format directly from USPTO at
CC seqdata.uspto.gov/sequence.html?DocID=20030118592. The authors have not
CC identified the sequences in the printed specification by their SEQ ID
CC number therefore none of the sequences can be explicitly identified.
XX
SQ Sequence 208 AA;

Query Match 100.0%; Score 593; DB 7; Length 208;
Best Local Similarity 100.0%; Pred. No. 1.9e-63;
Matches 116; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

```
Qy          1 FEAGAAAGAAPGEEDLCAAFNVICDNVGKDWRRLARQLKVSDTKIDSIEDRYPRNLTERV 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         82 FEAGAAAGAAPGEEDLCAAFNVICDNVGKDWRRLARQLKVSDTKIDSIEDRYPRNLTERV 141

Qy         61 RESLRIWKNTEKENATVAHLVGALRSCQMNLVADLVQEVQQARDLQNRSGAMSPMS 116
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        142 RESLRIWKNTEKENATVAHLVGALRSCQMNLVADLVQEVQQARDLQNRSGAMSPMS 197
```

RESULT 7
ADD25623
ID ADD25623 standard; protein; 208 AA.
XX
AC ADD25623;
XX
DT 15-JAN-2004 (first entry)
XX
DE Binding domain-immunoglobulin fusion protein-associated protein #89.
XX
KW Binding domain; immunoglobulin; fusion protein; cytostatic;
KW antiarthritic; immunosuppressive; antidiabetic; antithyroid;
KW neuroprotective; hinge region; immunoglobulin heavy chain;
KW CH2 constant region; CH3 constant region; IgG1;
KW antibody dependent cell-mediated cytotoxicity; ADCC; complement fixation;
KW malignant condition; B-cell disorder; melanoma; carcinoma; sarcoma;
KW rheumatoid arthritis; myasthenia gravis; Grave's disease;
KW type I diabetes mellitus; multiple sclerosis; autoimmune disease.
XX
OS Unidentified.
XX
PN US2003118592-A1.
XX
PD 26-JUN-2003.
XX
PF 25-JUL-2002; 2002US-00207655.
XX
PR 17-JAN-2001; 2001US-0367358P.
PR 17-JAN-2002; 2002US-00053530.
PR 03-JUN-2002; 2002US-0385691P.
XX
PA (GENE-) GENECRAFT INC.
XX
PI Ledbetter JA, Hayden-Ledbetter MS, Thompson PA;
XX
DR WPI; 2003-801317/75.
XX
PT New binding domain-immunoglobulin fusion protein, useful for treating a
PT subject having or suspected of having a malignant condition or a B-cell
PT disorder, e.g. melanoma, Grave's disease or autoimmune disease.
XX

PS Disclosure; SEQ ID NO 184; 157pp; English.
XX
CC The invention relates to a binding domain-immunoglobulin fusion protein
CC comprising a binding domain polypeptide that is fused to an
CC immunoglobulin hinge region polypeptide, an immunoglobulin heavy chain
CC CH2 constant region polypeptide that is fused to the hinge region
CC polypeptide, and an immunoglobulin heavy chain CH3 constant region
CC polypeptide that is fused to the CH2 constant region polypeptide. The
CC hinge region polypeptide comprises: a wild-type human IgG1 immunoglobulin
CC hinge region polypeptide; a mutated human IgG1 immunoglobulin hinge
CC region polypeptide, derived from (a) having 3 or more cysteine residues;
CC where the mutated human IgG1 immunoglobulin hinge region polypeptide
CC contains 2 cysteine residues, where the first cysteine is not mutated; a
CC mutated human IgG1 immunoglobulin hinge region polypeptide, derived from
CC (a) having 3 or more cysteine residues, where the mutated human IgG1
CC immunoglobulin hinge region polypeptide contains no more than one
CC cysteine residue; and a mutated human IgG1 immunoglobulin hinge region
CC polypeptide, derived from (a) having 3 or more cysteine residues; where
CC the mutated human IgG1 immunoglobulin hinge region polypeptide contains
CC no cysteine residues. The binding domain-immunoglobulin fusion protein is
CC capable of at least one immunological activity comprising antibody
CC dependent cell-mediated cytotoxicity (ADCC) and complement fixation. The
CC binding domain polypeptide is capable of specifically binding to an
CC antigen. Also included are an isolated polynucleotide encoding the
CC binding domain-immunoglobulin fusion protein, a recombinant expression
CC construct comprising the polynucleotide (operably linked to a promoter),
CC a host cell transformed or transfected with a recombinant expression
CC construct, producing the binding domain-immunoglobulin fusion protein, a
CC pharmaceutical composition comprising the binding domain-immunoglobulin
CC fusion protein or polynucleotide and a carrier, and treating a subject
CC having or suspected of having a malignant condition or a B-cell disorder.
CC The binding domain-immunoglobulin fusion protein is useful for treating a
CC subject having or suspected of having a malignant condition or a B-cell
CC disorder, e.g. melanoma, carcinoma or sarcoma, rheumatoid arthritis,
CC myasthenia gravis, Grave's disease, type I diabetes mellitus, multiple
CC sclerosis or autoimmune disease. The present sequence is a binding domain
CC -immunoglobulin fusion protein-associated protein sequence. Note: The
CC sequence data for this patent formed part of the printed specification
CC and is also available in electronic format directly from USPTO at
CC seqdata.uspto.gov/sequence.html?DocID=20030118592. The authors have not
CC identified the sequences in the printed specification by their SEQ ID
CC number therefore none of the sequences can be explicitly identified.
XX
SQ Sequence 208 AA;

Query Match 100.0%; Score 593; DB 7; Length 208;
Best Local Similarity 100.0%; Pred. No. 1.9e-63;
Matches 116; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 FEAGAAAGAAPGEEDLCAAFNVICDNVGKDWRRLARQLKVSDTKIDSIEDRYPRNLTERV 60
Db 82 FEAGAAAGAAPGEEDLCAAFNVICDNVGKDWRRLARQLKVSDTKIDSIEDRYPRNLTERV 141

Qy 61 RESLRIWKNTEKENATVAHLVGALRSCQMNLVADLVQEVQQARDLQNRSGAMSPMS 116
Db 142 RESLRIWKNTEKENATVAHLVGALRSCQMNLVADLVQEVQQARDLQNRSGAMSPMS 197

RESULT 8
ABM81285
ID ABM81285 standard; protein; 208 AA.
XX
AC ABM81285;
XX
DT 18-NOV-2004 (first entry)
XX
DE Tumour-associated antigenic target (TAT) polypeptide PRO4801, SEQ:3314.
XX
KW Tumour-associated antigenic target; TAT; human; overexpression; cancer;
KW tumour; diagnosis; cell proliferative disorder; breast cancer;
KW colorectal cancer; lung cancer; ovarian cancer; liver cancer;
KW central nervous system cancer; bladder cancer; pancreatic cancer;
KW cervical cancer; melanoma; leukaemia; hybridisation probe;
KW chromosome identification; chromosome mapping; gene mapping;
KW gene therapy; cytostatic.
XX
OS Homo sapiens.
XX
PN WO2004030615-A2.
XX
PD 15-APR-2004.
XX
PF 29-SEP-2003; 2003WO-US028547.
XX
PR 02-OCT-2002; 2002US-0414971P.
XX
PA (GETH) GENENTECH INC.
XX
PI Wu TD, Zhang Z, Zhou Y;
XX
DR WPI; 2004-347921/32.
DR N-PSDB; ACN39272.
XX
PT New tumor-associated antigenic target polypeptides and nucleic acids,
PT useful in preparing a medicament for treating or detecting a
PT proliferative disorder, e.g. breast, lung, colorectal, ovarian or
PT prostate cancer or tumor.
XX
PS Claim 12; SEQ ID NO 3314; 7273pp; English.
XX
CC The invention relates to human tumour-associated antigenic target (TAT)
CC polypeptides, and their related nucleic acids. The TAT polypeptides are
CC overexpressed in cancer tissues compared to normal tissues, and may thus
CC serve as effective targets for the diagnosis and treatment of cancer in
CC mammals. The invention also relates to nucleic acid and polypeptide
CC sequences at least 80% identical to the TAT nucleic acids and
CC polypeptides; expression vectors and host cells comprising a TAT nucleic
CC acid; an antibody specific for a TAT polypeptide; a peptide or organic
CC molecule which binds to a TAT polypeptide; fusion proteins comprising a
CC TAT polypeptide; and methods and compositions for the treatment or
CC diagnosis of cancer in mammals. TAT polypeptides, nucleic acids,
CC antibodies, antagonists, binding molecules and compositions are useful
CC for diagnosing or treating a cell proliferative disorder associated with
CC increased TAT expression, particularly cancers such as breast cancer,
CC colorectal cancer, lung cancer, ovarian cancer, liver cancer, bladder
CC cancer, pancreatic cancer, cervical cancer, cancers of the central
CC nervous system, melanoma and leukaemia. TAT nucleic acids may further be
CC used as hybridisation probes, in chromosome and gene mapping, in
CC chromosome identification and in gene therapy. The present sequence
CC represents a TAT polypeptide of the invention
XX
SQ Sequence 208 AA;

Query Match 100.0%; Score 593; DB 8; Length 208;
Best Local Similarity 100.0%; Pred. No. 1.9e-63;
Matches 116; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 FEAGAAAGAAPGEEDLCAAFNVICDNVGKDWRRLARQLKVSDTKIDSIEDRYPRNLTERV 60
Db 82 FEAGAAAGAAPGEEDLCAAFNVICDNVGKDWRRLARQLKVSDTKIDSIEDRYPRNLTERV 141

Qy 61 RESLRIWKNTEKENATVAHLVGALRSCQMNLVADLVQEVQQARDLQNRSGAMSPMS 116
Db 142 RESLRIWKNTEKENATVAHLVGALRSCQMNLVADLVQEVQQARDLQNRSGAMSPMS 197

RESULT 9
ADS88167
ID ADS88167 standard; protein; 208 AA.
XX
AC ADS88167;
XX
DT 18-NOV-2004 (first entry)
XX
DE Human protein of a TNF-alpha signalling pathway protein complex SeqID 22.
XX

KW protein complex; tumour necrosis factor-alpha signalling pathway;
KW TNF-alpha; chronic inflammatory disease; rheumatoid arthritis;
KW inflammatory bowel disease; infectious disease; septic shock;
KW bacterial infection; neurological disease; stroke-induced inflammation;
KW neurodegenerative disease; cancer; antiinflammatory; antiarthritic;
KW antirheumatic; cytostatic; antibacterial; gene therapy; human.
XX
OS Homo sapiens.
XX
PN WO2004035783-A2.
XX
PD 29-APR-2004.
XX
PF 24-SEP-2003; 2003WO-EP050655.
XX
PR 26-SEP-2002; 2002EP-00021809.
PR 10-FEB-2003; 2003EP-00100274.
XX
PA (CELL-) CELLZOME AG.
XX
PI Bouwmeester T, Huhse B, Bauch A, Ruffner H, Bauer A, Kuester B;
PI Superti-Furga G, Kruse U;
XX
DR WPI; 2004-348460/32.
XX
PT New protein complex comprising at least one first and second protein of
PT the Tumor Necrosis Factor-alpha(TNF-alpha)-signaling pathway, useful for
PT diagnosing or treating inflammation, neurological diseases, infectious
PT diseases or cancer.
XX
PS Example; SEQ ID NO 22; 1980pp; English.
XX
CC This invention relates to novel protein complexes of the tumour necrosis
CC factor-alpha (TNF-alpha) signalling pathway. Specifically, it refers to
CC methods for preparing these complexes comprising at least two component
CC proteins, as well as screening methods to identify modulators of the
CC pathway, which include antibodies, agonists and antagonists thereof. The
CC present invention describes a protein complex and kit that are useful for
CC diagnosing, prognosing or treating chronic inflammatory diseases such as
CC rheumatoid arthritis and inflammatory bowel disease; infectious diseases
CC such as septic shock and bacterial infections; neurological diseases such
CC as stroke-induced inflammation in neurons; neurodegenerative diseases and
CC cancer. Accordingly, these complexes can be used for the development of
CC pharmaceutical compositions that exhibit antiinflammatory, antiarthritic,
CC antirheumatic, cytostatic and antibacterial activities and can be used
CC for gene therapy purposes. In particular, the invention further provides
CC siRNA-oligonucleotides useful for inhibiting protein expression for in
CC vitro or cell culture assays. This polypeptide is a human protein that
CC can be used in combination with other proteins provided in the
CC specification to form novel complexes of the TNF-alpha signalling pathway
CC of the invention.
XX
SQ Sequence 208 AA;

Query Match 100.0%; Score 593; DB 8; Length 208;
Best Local Similarity 100.0%; Pred. No. 1.9e-63;
Matches 116; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 FEAGAAAGAAPGEEDLCAAFNVICDNVGKDWRRLARQLKVSDTKIDSIEDRYPRNLTERV 60
||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db 82 FEAGAAAGAAPGEEDLCAAFNVICDNVGKDWRRLARQLKVSDTKIDSIEDRYPRNLTERV 141

Qy 61 RESLRIWKNTEKENATVAHLVGALRSCQMNLVADLVQEVQQARDLQNRSGAMSPMS 116
||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db 142 RESLRIWKNTEKENATVAHLVGALRSCQMNLVADLVQEVQQARDLQNRSGAMSPMS 197

RESULT 10
ADD25847
ID ADD25847 standard; protein; 211 AA.
XX
AC ADD25847;
XX
DT 15-JAN-2004 (first entry)
XX
DE Binding domain-immunoglobulin fusion protein-associated protein #183.
XX
KW Binding domain; immunoglobulin; fusion protein; cytostatic;
KW antiarthritic; immunosuppressive; antidiabetic; antithyroid;
KW neuroprotective; hinge region; immunoglobulin heavy chain;
KW CH2 constant region; CH3 constant region; IgG1;
KW antibody dependent cell-mediated cytotoxicity; ADCC; complement fixation;
KW malignant condition; B-cell disorder; melanoma; carcinoma; sarcoma;
KW rheumatoid arthritis; myasthenia gravis; Grave's disease;
KW type I diabetes mellitus; multiple sclerosis; autoimmune disease.
XX
OS Unidentified.
XX
PN US2003118592-A1.
XX
PD 26-JUN-2003.
XX
PF 25-JUL-2002; 2002US-00207655.
XX
PR 17-JAN-2001; 2001US-0367358P.
PR 17-JAN-2002; 2002US-00053530.
PR 03-JUN-2002; 2002US-0385691P.
XX
PA (GENE-) GENECRAFT INC.
XX
PI Ledbetter JA, Hayden-Ledbetter MS, Thompson PA;
XX
DR WPI; 2003-801317/75.
XX
PT New binding domain-immunoglobulin fusion protein, useful for treating a
PT subject having or suspected of having a malignant condition or a B-cell
PT disorder, e.g. melanoma, Grave's disease or autoimmune disease.
XX
PS Disclosure; SEQ ID NO 408; 157pp; English.
XX
CC The invention relates to a binding domain-immunoglobulin fusion protein
CC comprising a binding domain polypeptide that is fused to an
CC immunoglobulin hinge region polypeptide, an immunoglobulin heavy chain
CC CH2 constant region polypeptide that is fused to the hinge region
CC polypeptide, and an immunoglobulin heavy chain CH3 constant region
CC polypeptide that is fused to the CH2 constant region polypeptide. The
CC hinge region polypeptide comprises: a wild-type human IgG1 immunoglobulin
CC hinge region polypeptide; a mutated human IgG1 immunoglobulin hinge
CC region polypeptide, derived from (a) having 3 or more cysteine residues;
CC where the mutated human IgG1 immunoglobulin hinge region polypeptide
CC contains 2 cysteine residues, where the first cysteine is not mutated; a
CC mutated human IgG1 immunoglobulin hinge region polypeptide, derived from
CC (a) having 3 or more cysteine residues, where the mutated human IgG1
CC immunoglobulin hinge region polypeptide contains no more than one
CC cysteine residue; and a mutated human IgG1 immunoglobulin hinge region
CC polypeptide, derived from (a) having 3 or more cysteine residues; where
CC the mutated human IgG1 immunoglobulin hinge region polypeptide contains
CC no cysteine residues. The binding domain-immunoglobulin fusion protein is
CC capable of at least one immunological activity comprising antibody
CC dependent cell-mediated cytotoxicity (ADCC) and complement fixation. The
CC binding domain polypeptide is capable of specifically binding to an
CC antigen. Also included are an isolated polynucleotide encoding the
CC binding domain-immunoglobulin fusion protein, a recombinant expression
CC construct comprising the polynucleotide (operably linked to a promoter),
CC a host cell transformed or transfected with a recombinant expression
CC construct, producing the binding domain-immunoglobulin fusion protein, a
CC pharmaceutical composition comprising the binding domain-immunoglobulin
CC fusion protein or polynucleotide and a carrier, and treating a subject
CC having or suspected of having a malignant condition or a B-cell disorder.
CC The binding domain-immunoglobulin fusion protein is useful for treating a
CC subject having or suspected of having a malignant condition or a B-cell
CC disorder, e.g. melanoma, carcinoma or sarcoma, rheumatoid arthritis,
CC myasthenia gravis, Grave's disease, type I diabetes mellitus, multiple
CC sclerosis or autoimmune disease. The present sequence is a binding domain
CC -immunoglobulin fusion protein-associated protein sequence. Note: The
CC sequence data for this patent formed part of the printed specification

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CC   and is also available in electronic format directly from USPTO at
CC   seqdata.uspto.gov/sequence.html?DocID=20030118592. The authors have not
CC   identified the sequences in the printed specification by their SEQ ID
CC   number therefore none of the sequences can be explicitly identified.
XX
SQ   Sequence 211 AA;

  Query Match             100.0%;  Score 593;  DB 7;  Length 211;
  Best Local Similarity   100.0%;  Pred. No. 1.9e-63;
  Matches  116;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 FEAGAAAGAAPGEEDLCAAFNVICDNVGKDWRRLARQLKVSDTKIDSIEDRYPRNLTERV 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         85 FEAGAAAGAAPGEEDLCAAFNVICDNVGKDWRRLARQLKVSDTKIDSIEDRYPRNLTERV 144

Qy         61 RESLRIWKNTEKENATVAHLVGALRSCQMNLVADLVQEVQQARDLQNRSGAMSPMS 116
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        145 RESLRIWKNTEKENATVAHLVGALRSCQMNLVADLVQEVQQARDLQNRSGAMSPMS 200


RESULT 11
AAR98346
ID   AAR98346 standard; protein; 256 AA.
XX
AC   AAR98346;
XX
DT   13-SEP-1996  (first entry)
XX
DE   MORT-1 modulator of FAS receptor.
XX
KW   MORT-1; HF1; FAS/APO1 receptor; FAS-R; tumour; cancer; HIV;
KW   mediator of receptor toxicity; gene therapy.
XX
OS   Homo sapiens.
XX
FH   Key             Location/Qualifiers
FT   Domain          160. .221
FT                   /label= Death domain
XX
PN   WO9618641-A1.
XX
PD   20-JUN-1996.
XX
PF   14-DEC-1995;   95WO-US016542.
XX
PR   15-DEC-1994;   94IL-00112022.
PR   19-FEB-1995;   95IL-00112692.
PR   16-JUL-1995;   95IL-00114615.
XX
PA   (YEDA ) YEDA RES & DEV CO LTD.
PA   (WEIN/) WEINWURZEL H.
XX
PI   Wallach D,  Boldin M,  Varfolomeev E,  Mett I;
XX
DR   WPI; 1996-300569/30.
DR   N-PSDB; AAT30372.
XX
PT   MORT-1 protein capable of interacting with FAS-R intracellular domain -
PT   useful for modulating FAS-R ligand effect on cells and treating, e.g.
PT   tumour cells and HIV-infected cells.
XX
PS   Claim 5; Fig 4; 72pp; English.
XX
CC   MORT-1 (AAR98346) (Mediator of Receptor Toxicity), also designated HF1,
CC   is a novel protein that binds to the intracellular domain (Fas-IC) of the
CC   FAS ligand receptor FAS-R (or FAS/APO1), and is capable of modulating the
CC   function of Fas-R. MORT-1 is also capable of self-association and can
CC   activate cell cytotoxicity on its own. Recombinant MORT-1 can be obtd.
CC   from host cells transformed with a vector carrying a cDNA clone
CC   (AAT30372) isolated from HeLa cells. MORT-1 can be used to modulate the
CC   FAS-R ligand on cells carrying an FAS-R. It can also be used to treat
CC   tumour cells or HIV-infected cells, or to raise antibodies
XX
SQ   Sequence 256 AA;

  Query Match             100.0%;  Score 593;  DB 2;  Length 256;
  Best Local Similarity   100.0%;  Pred. No. 2.5e-63;
  Matches  116;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 FEAGAAAGAAPGEEDLCAAFNVICDNVGKDWRRLARQLKVSDTKIDSIEDRYPRNLTERV 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        130 FEAGAAAGAAPGEEDLCAAFNVICDNVGKDWRRLARQLKVSDTKIDSIEDRYPRNLTERV 189

Qy         61 RESLRIWKNTEKENATVAHLVGALRSCQMNLVADLVQEVQQARDLQNRSGAMSPMS 116
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        190 RESLRIWKNTEKENATVAHLVGALRSCQMNLVADLVQEVQQARDLQNRSGAMSPMS 245


RESULT 12
AAW11894
ID   AAW11894 standard; protein; 256 AA.
XX
AC   AAW11894;
XX
DT   25-MAR-2003  (revised)
DT   29-OCT-1997  (first entry)
XX
DE   Modulator of cellular toxicity (MORT-1).
XX
KW   MACH; MORT-1 binding protein; mediator of receptor toxicity; cell death;
KW   antibody; FAS ligand receptor; FAS-R; death domain region; septic shock;
KW   tumour necrosis factor; tumour; HIV-infection; oligodendrocyte death;
KW   apoptosis/programmed cell death; p55-R; graft rejection; acute hepatitis;
KW   autoimmune disease; multiple sclerosis; AIDS-inhibited T-cell suicide;
KW   TNF; therapy.
XX
OS   Homo sapiens.
XX
PN   WO9703998-A1.
XX
PD   06-FEB-1997.
XX
PF   14-JUN-1996;   96WO-US010521.
XX
PR   16-JUL-1995;   95IL-00114615.
PR   17-AUG-1995;   95IL-00114986.
PR   14-SEP-1995;   95IL-00115319.
PR   27-DEC-1995;   95IL-00116588.
PR   16-APR-1996;   96IL-00117932.
XX
PA   (YEDA ) YEDA RES & DEV CO LTD.
PA   (WEIN/) WEINWURZEL H.
XX
PI   Wallach D,  Boldin M,  Goncharov T,  Goltsev YV;
XX
DR   WPI; 1997-132570/12.
DR   N-PSDB; AAT61397.
XX
PT   New DNA encoding MACH protein that interacts with MORT-1 protein - to
PT   mediate intracellular effects of FAS or TNF receptors, partic. for
PT   regulating apoptosis in tumours, virus-infected cells etc.
XX
PS   Disclosure; Page 102-103; 163pp; English.
XX
CC   This sequence represents the mediator of cellular toxicity (MORT-1)
CC   protein. This sequence is bound by the protein of the invention (see
CC   AAW11892), designated MACH. MORT-1 binds to the FAS ligand receptor (FAS-
CC   R) death domain region, and triggers part of the cell death signalling
CC   cascade in mammalian cells. Vectors containing MACH, the MACH protein,
CC   and antibodies (Ab) against it are used to modulate the effect of FAS-R
CC   ligand or TNF on cells that carry FAS-R or p55-R. This is specifically
CC   for treating tumours, HIV-infected cells or other diseased cells, by
CC   control of apoptosis/programmed cell death. The MACH protein is a
CC   mediator of the cell death pathway initiated by TNF and FAS-R binding,
CC   i.e. it mimics or enhances the effect of MORT-1 where increased
CC   cytotoxicity is required. To inhibit the effect of MORT-1, e.g. in cases
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CC   of septic shock, graft rejection and acute hepatitis, sequences encoding
CC   antisense molecules or ribozymes, or Ab against MACH, are used. Compounds
CC   that inhibit MACH are potentially useful for controlling MACH activity
CC   e.g. in cases of autoimmune disease, oligodendrocyte death in multiple
CC   sclerosis or AIDS-inhibited T-cell suicide. The MACH protein can also be
CC   used to isolate and characterise other proteins and receptors involved in
CC   signalling and for Ab production. The Ab can be used to purify the new
CC   proteins and for diagnosis of conditions involving abnormal function of
CC   FAS-R mediated cellular effects. (Updated on 25-MAR-2003 to correct PR
CC   field.)
XX
SQ   Sequence 256 AA;

  Query Match             100.0%;  Score 593;  DB 2;  Length 256;
  Best Local Similarity   100.0%;  Pred. No. 2.5e-63;
  Matches  116;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 FEAGAAAGAAPGEEDLCAAFNVICDNVGKDWRRLARQLKVSDTKIDSIEDRYPRNLTERV 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        130 FEAGAAAGAAPGEEDLCAAFNVICDNVGKDWRRLARQLKVSDTKIDSIEDRYPRNLTERV 189

Qy         61 RESLRIWKNTEKENATVAHLVGALRSCQMNLVADLVQEVQQARDLQNRSGAMSPMS 116
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        190 RESLRIWKNTEKENATVAHLVGALRSCQMNLVADLVQEVQQARDLQNRSGAMSPMS 245


RESULT 13
AAW87492
ID   AAW87492 standard; protein; 201 AA.
XX
AC   AAW87492;
XX
DT   12-FEB-1999  (first entry)
XX
DE   Amino acid sequence of MORT1 isoform MORT1del21 from human brain.
XX
KW   MORT1; MORT1del21; NTERA2; CNS; isoform; death domain; Fas/APO1;
KW   MACH alpha1; ICE/Ced3; caspase; anti-apoptopic; gene therapy;
KW   in vivo agent; neuronal apoptosis; human.
XX
OS   Homo sapiens.
XX
PN   WO9849297-A1.
XX
PD   05-NOV-1998.
XX
PF   14-APR-1998;   98WO-US007439.
XX
PR   25-APR-1997;   97US-0044835P.
XX
PA   (AMHP ) AMERICAN HOME PROD CORP.
XX
PI   Bingham BW,  Young KH,  Wood AT,  Birsan C;
XX
DR   WPI; 1999-009424/01.
DR   N-PSDB; AAV71929.
XX
PT   Human, neuronal MORT1 iso:form(s) - used as screening agents in
PT   diagnosing CNS diseases, and in discovering CNS-specific anti-apoptopic
PT   compounds.
XX
PS   Claim 6; Page 28-29; 31pp; English.
XX
CC   This represents the amino acid sequence of a MORT1 isoform MORT1del21.
CC   The encoding cDNA was isolated from human brain and deposited under the
CC   accession number ATCC 209018. The cDNA has a 21 base pair deletion as
CC   compared to the published MORT1 sequence (bp 172-192 of the coding
CC   sequence). The invention relates to three MORT1 nucleic acid isoforms
CC   (AAV71928 to AAV71930) that encode proteins which can interact with the
CC   death domain of Fas/APO1. The MORT1 isoforms can also interact with MACH
CC   alpha1 or other members of the ICE/Ced3 (Caspase) family of proteins. The
CC   transcript isoforms, together with their encoded proteins are useful as
CC   screening agents in diagnosing CNS diseases, and in discovering CNS-
CC   specific anti-apoptopic compounds. They are useful in gene therapy either
CC   as in vivo agents in humans or as experimental tools in manipulating
CC   neuronal apoptosis in cell culture and animal model systems
XX
SQ   Sequence 201 AA;

  Query Match             99.3%;  Score 589;  DB 2;  Length 201;
  Best Local Similarity   99.1%;  Pred. No. 5.6e-63;
  Matches  115;  Conservative    0;  Mismatches    1;  Indels    0;  Gaps    0;

Qy          1 FEAGAAAGAAPGEEDLCAAFNVICDNVGKDWRRLARQLKVSDTKIDSIEDRYPRNLTERV 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         75 FEAGAAAGAAPGEEDLCAAFNVICDNVGKDWRRLARQLKVSDTKIDSIEDRYPRNLTERV 134

Qy         61 RESLRIWKNTEKENATVAHLVGALRSCQMNLVADLVQEVQQARDLQNRSGAMSPMS 116
              |||||||||||||||||||||||||||| ||||||||||||||||||||||||||
Db        135 RESLRIWKNTEKENATVAHLVGALRSCQMNLAADLVQEVQQARDLQNRSGAMSPMS 190


RESULT 14
AAW87493
ID   AAW87493 standard; protein; 208 AA.
XX
AC   AAW87493;
XX
DT   12-FEB-1999  (first entry)
XX
DE   Amino acid sequence of MORT1 isoform MORT1G173A from human brain.
XX
KW   MORT1; MORT1del21; NTERA2; CNS; isoform; death domain; Fas/APO1;
KW   MACH alpha1; ICE/Ced3; caspase; anti-apoptopic; gene therapy;
KW   in vivo agent; neuronal apoptosis; human.
XX
OS   Homo sapiens.
XX
PN   WO9849297-A1.
XX
PD   05-NOV-1998.
XX
PF   14-APR-1998;   98WO-US007439.
XX
PR   25-APR-1997;   97US-0044835P.
XX
PA   (AMHP ) AMERICAN HOME PROD CORP.
XX
PI   Bingham BW,  Young KH,  Wood AT,  Birsan C;
XX
DR   WPI; 1999-009424/01.
DR   N-PSDB; AAV71930.
XX
PT   Human, neuronal MORT1 iso:form(s) - used as screening agents in
PT   diagnosing CNS diseases, and in discovering CNS-specific anti-apoptopic
PT   compounds.
XX
PS   Claim 7; Page 30-31; 31pp; English.
XX
CC   This represents the amino acid sequence of a MORT1 isoform MORT1G173A.
CC   The encoding cDNA was isolated from human brain and deposited under the
CC   accession number ATCC 209019. The cDNA has a nucleotide substitution (G
CC   to A) at basepair position 173 of the published MORT1 coding sequence.
CC   The invention relates to three MORT1 nucleic acid isoforms (AAV71928 to
CC   AAV71930) that encode proteins which can interact with the death domain
CC   of Fas/APO1. The MORT1 isoforms can also interact with MACH alpha1 or
CC   other members of the ICE/Ced3 (Caspase) family of proteins. The
CC   transcript isoforms, together with their encoded proteins are useful as
CC   screening agents in diagnosing CNS diseases, and in discovering CNS-
CC   specific anti- apoptopic compounds. They are useful in gene therapy
CC   either as in vivo agents in humans or as experimental tools in
CC   manipulating neuronal apoptosis in cell culture and animal model systems
XX
SQ   Sequence 208 AA;

  Query Match             99.3%;  Score 589;  DB 2;  Length 208;
```

```
  Best Local Similarity   99.1%;  Pred. No. 5.8e-63;
  Matches  115;  Conservative    0;  Mismatches    1;  Indels    0;  Gaps    0;

Qy          1 FEAGAAAGAAPGEEDLCAAFNVICDNVGKDWRRLARQLKVSDTKIDSIEDRYPRNLTERV 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         82 FEAGAAAGAAPGEEDLCAAFNVICDNVGKDWRRLARQLKVSDTKIDSIEDRYPRNLTERV 141

Qy         61 RESLRIWKNTEKENATVAHLVGALRSCQMNLVADLVQEVQQARDLQNRSGAMSPMS 116
              ||||||||||||||||||||||||||| ||||||||||||||||||||||||
Db        142 RESLRIWKNTEKENATVAHLVGALRSCQMNLAADLVQEVQQARDLQNRSGAMSPMS 197


RESULT 15
AAW87491
ID   AAW87491 standard; protein; 201 AA.
XX
AC   AAW87491;
XX
DT   12-FEB-1999  (first entry)
XX
DE   Amino acid sequence of MORT1 isoform MORT1del21 from NTERA2 cells.
XX
KW   MORT1; MORT1del21; NTERA2; CNS; isoform; death domain; Fas/APO1;
KW   MACH alpha1; ICE/Ced3; caspase; anti-apoptopic; gene therapy;
KW   in vivo agent; neuronal apoptosis; human.
XX
OS   Homo sapiens.
XX
PN   WO9849297-A1.
XX
PD   05-NOV-1998.
XX
PF   14-APR-1998;   98WO-US007439.
XX
PR   25-APR-1997;   97US-0044835P.
XX
PA   (AMHP ) AMERICAN HOME PROD CORP.
XX
PI   Bingham BW,  Young KH,  Wood AT,  Birsan C;
XX
DR   WPI; 1999-009424/01.
DR   N-PSDB; AAV71928.
XX
PT   Human, neuronal MORT1 iso:form(s) - used as screening agents in
PT   diagnosing CNS diseases, and in discovering CNS-specific anti-apoptopic
PT   compounds.
XX
PS   Claim 5; Page 26-27; 31pp; English.
XX
CC   This represents the amino acid sequence of a MORT1 isoform MORT1del21.
CC   The encoding cDNA was isolated from NTERA2 cells and deposited under the
CC   accession number ATCC 209013. The cDNA has a 21 base pair deletion as
CC   compared to the published MORT1 sequence (bp 172-192 of the coding
CC   sequence). The invention relates to three MORT1 nucleic acid isoforms
CC   (AAV71928 to AAV71930) that encode proteins which can interact with the
CC   death domain of Fas/APO1. The MORT1 isoforms can also interact with MACH
CC   alpha1 or other members of the ICE/Ced3 (Caspase) family of proteins. The
CC   transcript isoforms, together with their encoded proteins are useful as
CC   screening agents in diagnosing CNS diseases, and in discovering CNS-
CC   specific anti-apoptopic compounds. They are useful in gene therapy either
CC   as in vivo agents in humans or as experimental tools in manipulating
CC   neuronal apoptosis in cell culture and animal model systems
XX
SQ   Sequence 201 AA;

  Query Match             98.8%;  Score 586;  DB 2;  Length 201;
  Best Local Similarity   99.1%;  Pred. No. 1.3e-62;
  Matches  115;  Conservative    0;  Mismatches    1;  Indels    0;  Gaps    0;

Qy          1 FEAGAAAGAAPGEEDLCAAFNVICDNVGKDWRRLARQLKVSDTKIDSIEDRYPRNLTERV 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         75 FEAGAAAGAAPGEEDLCAAFNVICDNVGKDWRRLARQLKVSDTKIDSIEDRYPRNLTERV 134

Qy         61 RESLRIWKNTEKENATVAHLVGALRSCQMNLVADLVQEVQQARDLQNRSGAMSPMS 116
              ||||||||||||||||||||||||||| ||||||||||||||||||||||||
Db        135 RESLRIWKNTEKENATVAHLVGALRSCQMNLVADLVQGVQQARDLQNRSGAMSPMS 190

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Job time : 79 secs
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